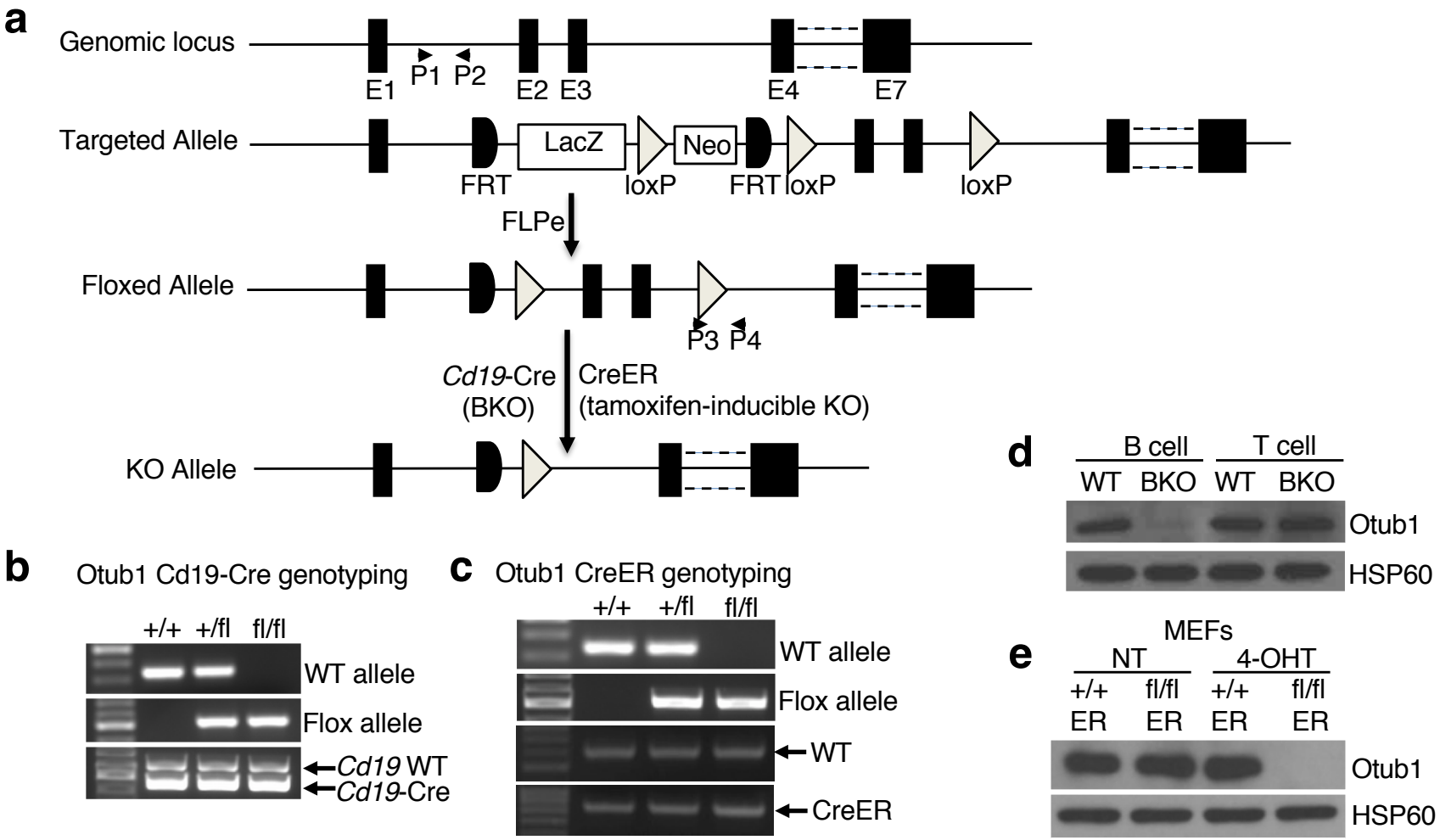

Fig. S2. Generation of *Otub1*-BKO and inducible KO mice. **a** Schematic of *Otub1* gene targeting using an FRT-LoxP vector. Targeted mice were crossed with FRT deleter (Rosa26-FLPe) mice to generate *Otub1*-floxed mice, which were further crossed with Cre mice to generate BKO (*Cd19*-Cre) and tamoxifen-inducible KO (CreER) mice. **b** Genotyping PCR analysis of $Otub1^{+/+}$(+/+), $Otub1^{+/fl}$ (+/fl), and $Otub1^{fl/fl}$ (fl/fl) mice crossed with *Cd19*-Cre mice (all with *Cd19*-Cre/+ heterozygous genotype), showing wildtype (WT) and flox alleles of *Otub1* gene as well as *Cd19* wildtype and *Cd19*-Cre fusion gene locus. **c** Genotyping PCR analysis of $Otub1^{+/+}$(+/+), $Otub1^{+/fl}$ (+/fl), and $Otub1^{fl/fl}$ (fl/fl) mice crossed with CreER mice (all with CreER/+ heterozygous genotype), showing wildtype (WT) and flox alleles of *Otub1* gene as well as wildtype (WT) and CreER alleles of the Cre insertion locus. **d,e** Immunoblot analysis of Otub1 and loading control HSP60 in B and T cells of the BKO or wildtype control mice (**d**) or in $Otub1^{+/+}$CreER (+/+ ER) or $Otub1^{fl/fl}$Cre-ER (fl/fl ER) MEFs either not treated (NT) or induced with the tamoxifen metabolite 4-hydroxytamoxifen (4-OHT) (**e**).